

COMPUTER AIDED PERIPHERAL ARTERIAL DISEASE DIAGNOSIS AND BLOOD PRESSURE ESTIMATION VIA PULSE OSCILLATION

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ABSTRACT

Peripheral arterial disease (PAD) is a collective term for all diseases caused by the obstruction of large peripheral arteries. Early diagnosis allows for faster treatment and the reduction of further tissue destruction.

In this paper we present a novel approach for early PAD diagnosis based on the pulse oscillation measurement of any extremity. In contrast to standard pulse oscillography we record all pulse oscillations during intervals of five seconds at constant cuff pressures. Different statistical parameters describing the single pressure steps are then used as features to automatically classify PAD positive and negative persons. We evaluate nine features that are extracted from a pre-classified data pool containing the pressure step oscillograms (PSOs) of 50 healthy and 50 ill persons. By means of receiver operation characteristic (ROC) analysis the most promising features for classification are determined. Additionally, the systolic and diastolic blood pressure is automatically deduced from the feature showing the best classification performance.

1. INTRODUCTION

Peripheral arterial disease (PAD) is a collective term for all diseases caused by the obstruction of large peripheral arteries which exemplary can result from atherosclerosis. PAD always causes ischemia, which causes patients to suffer from increasing pain in the extremities and thus restricts their mobility. Finally, PAD can lead to heart failure and exitus. About 20% to 30% of people older than 65 years suffer from PAD. Alarmingly, PAD is detected in only 5% of all affected persons! [1][2]

Early diagnosis allows for faster treatment and, thus, reduction of further tissue destruction. The most common first-line test for screening is determining the Ankle-Brachial-Index (ABI). To do this, the systolic blood pressures at the patient's arms and legs are measured via Doppler sonography. The ABI is calculated by dividing the systolic ankle pressure by the higher of the two systolic blood pressures in the arms. An ABI between 1 and 1.5 is normal, a value smaller than 0.9 indicates a PAD positive person. Another accepted PAD screening method is capturing pulse waves at the wrists and shackles or fingers and toes via pulse oscillation. Based on the measured pulse oscillations the oscillometric Wrist-Shackle-Index (oWSI) or Finger-Toe-Index (oFTI) is determined. These indices are calculated by dividing the mean arterial pressure (oscillometric index) of the shackle or toe by that of the wrist or finger. The interpretation of these ratios is similar to that of the ABI. [3][4]

The reliability of the ABI method strongly depends on the skill of the examiner in accurately finding the blood vessels and correctly performing the sonography [1]. Furthermore, with both methods two measurements (arm/leg or wrist/shackle) are necessary which appears to be time-consuming and error-prone.

In this paper we present a novel approach similar to that one proposed by Colak and Isic [8] which is based on the classification of features extracted from pulse oscillations, whereby we put our focus on different features and other classification techniques. Our approach is based on the pulse oscillation measurement of any extremity. In contrast to standard pulse oscillography, we record all

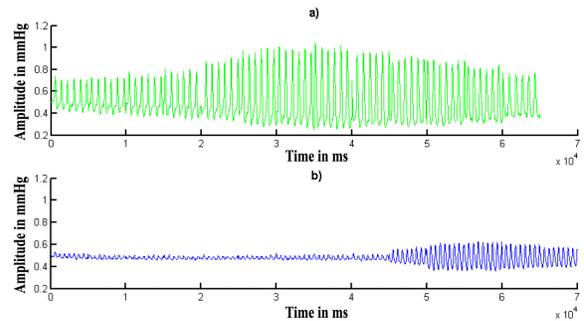


Figure 1: Pressure step oscillograms of a) healthy persons, b) PAD patients.

pulse oscillations during intervals of five seconds at constant cuff pressures. Doing so over the whole range of relevant cuff pressures leads to pressure step oscillograms (PSOs) as shown in Figure 1.

Healthy persons show low oscillations with high pressures at the beginning as well as with low pressures at the end of the examination. In the center of the range - around the mean arterial pressure - oscillations show the highest amplitudes. However, in persons who suffer from PAD such a dynamic is missing and, if at all, higher amplitudes only appear with low pressures.

Based on this knowledge we have developed a new and easy method for PAD diagnoses by automatically interpreting statistical parameters extracted from pressure step oscillograms as shown above. In this context elementary parameters like mean value, standard deviation, area or energy are extracted as pressure step features from a set of representative test data and are used for automatic patient classification (ill or healthy). The results are compared to clearly diag-nosed reference values.

Hypertonia belongs to the established risk factors as well as to the side-effects of a PAD. Thus, another related and even obvious objective is the determination of the systolic and diastolic blood pressure from the best pre-selected pressure step feature. For this purpose, feature thresholds for automatic blood pressure estimation are empirically determined by cross validating given test data. Afterwards, the applicability of these thresholds is evaluated by comparing the automatically determined blood pressures of 20 test persons to those provided by a standard sphygmomanometer (SM). This method is currently restricted to healthy persons only.

2. MATERIALS & METHODS

We introduce algorithms for extracting PSO features that are promising for automatic PAD positive or negative classification and healthy persons' blood pressure estimation. Additionally, we describe the structure of PSO data sets and the source of reference values used for evaluating our approaches.

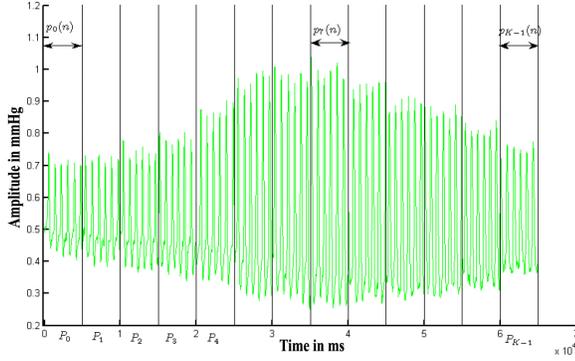


Figure 2: PSO of a healthy person. Discrete pressure step signals $p_k(n)$ of different pressure steps P_k are subdivided by vertical lines. $P_{\max}=140\text{mmHg}$, $P_{\min}=20\text{mmHg}$, $\Delta P=10\text{mmHg}$.

2.1 Diagnosis of Peripheral Arterial Disease

First, we show how it is possible to distinguish between ill and healthy persons using features extracted from pressure step oscillograms.

2.1.1 Pressure Step Oscillograms (PSOs)

Figure 2 shows a PSO and gives an overview of the parameters introduced in this section. A PSO of a single person is the set $p_k(n)$ of K discrete pulse oscillation signals $p_k(n)$ at different cuff pressures P_k . Starting from the maximum cuff pressure $P_0 = P_{\max}$ in the first pressure step, the cuff pressure is consecutively decreased by the constant pressure difference ΔP . In the last pressure step the minimum pressure $P_K = P_{\min}$ is reached. Hence, the PSO consists of $K = (P_{\max} - P_{\min})/\Delta P$ distinct pressure steps. The pressure of the k -th pressure step is given by $P_k = P_{\max} - k \cdot \Delta P$, $k \in 0 \dots K - 1$.

The pulse oscillation at constant cuff pressure is sampled with 1kHz over a time interval of 5s. This results in a discrete pressure step signal $p_k(n)$ of length $N=5000$.

2.1.2 PSO Data Sets

For the algorithm evaluation 30 PSOs are recorded at the toes of test persons. The data sets are pre-classified as PAD positive or negative by physicians. For further analysis 50 clearly positive and 50 clearly negative data sets are selected, resulting in a total of $M=100$ data sets.

2.1.3 Pressure Step Features

For accurately describing a PSO, pressure step features f_k are calculated from the oscillations $p_k(n)$ of every pressure step k . We evaluate the following nine features according to their capability to correctly classify PAD positives and negatives:

- Minimum: $p_k^{\min} = \min_n p_k(n)$,
- Maximum: $p_k^{\max} = \max_n p_k(n)$,
- Sample Mean Value: $\mu_k = \frac{1}{N} \sum_{n=1}^N p_k(n)$,
- Sample Std. Dev.: $\sigma_k = \sqrt{\frac{1}{N-1} \sum_{n=1}^N (p_k(n) - \mu_k)^2}$,
- Skewness: $S_k = \frac{1}{N} \sum_{n=1}^N \left(\frac{p_k(n) - \mu_k}{\sigma_k} \right)^3$,
- Kurtosis: $K_k = \frac{1}{N} \sum_{n=1}^N \left(\frac{p_k(n) - \mu_k}{\sigma_k} \right)^4$,
- Area: $A_k = \sum_{n=1}^N |p_k(n) - \mu_k|$,

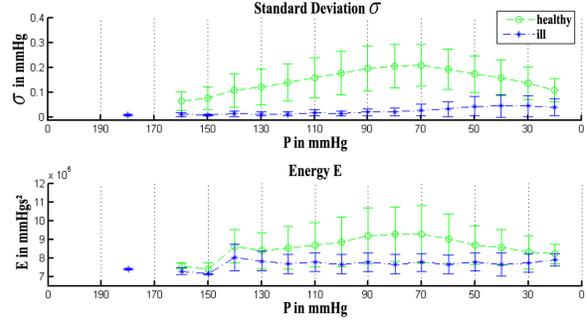


Figure 3: Mean values $\mu^{f,K}$ (marker) and corresponding standard deviations $\sigma^{f,K}$ (bar) for all pressure steps of features σ and E for ill and healthy persons, respectively.

- Energy: $E_k = \sum_{n=1}^N p_k(n)^2$,
- Entropy: $H_k = - \sum_{n=1}^N p_n \cdot \log(n)$.

For all K pressure steps and all M data sets the features $f_{k,m}$ are computed, whereby m denotes the data set index. To see how the pressure step features distinguish between ill and healthy persons, their mean values $\mu^{f,K}$ and standard deviations $\sigma^{f,K}$ are calculated for each pressure step k over all data sets of ill and healthy persons, respectively.

$$\mu_k^{f,K} = \frac{1}{M} \cdot \sum_{m=1}^M f_{k,m}$$

$$\sigma_k^{f,K} = \sqrt{\frac{1}{M} \cdot \sum_{m=1}^M (f_{k,m} - \mu_k^{f,K})^2}$$

Figure 3 exemplarily shows the resulting curves for the features Standard Deviation σ and Energy E .

2.1.4 Data Set Features

Every data set is now described by K pressure step features that, in principle, can directly be used for classification. However, using such high dimensional feature vectors is not feasible, because the classification complexity drastically increases. Thus, we average the pressure step features $f_{k,m}$ over all K pressure steps per data set to obtain more compact data set feature

$$\mu_m^{f,M} = \frac{1}{K} \sum_{k=1}^K f_{k,m}$$

Figure 4 shows the pressure step features σ and the corresponding data set features $\mu^{\sigma,M}$ for one healthy and one ill person, respectively.

2.1.5 Data Set Feature Evaluation

In order to determine which data set feature(s) $\mu^{f,M}$ yield the best classification performance (ill/healthy), we compare the features' receiver operation characteristics (ROC). Figure 5 shows the probability density functions of the data set features $\mu^{\sigma,M}$ and $\mu^{E,M}$ for the data sets that represent ill (dash-dotted) and healthy (dashed) persons.

The ROC coordinate system is spanned by the sensitivity (probability of correctly classified features belonging to class ill) and the specificity (probability of correctly classified features belonging to class healthy). Sensitivity and specificity are functions of the threshold used for classification (vertical line in Figure 5). They are determined for each data set feature separately. The thresholds are

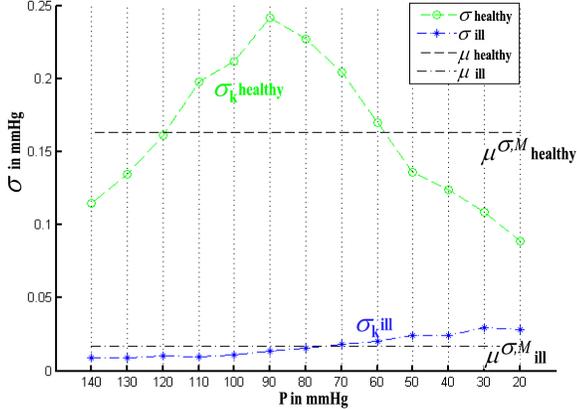


Figure 4: Pressure step feature σ for one healthy and one ill person. The dashed horizontal lines correspond to the respective data set features $\mu^{\sigma,M}$ (mean values).

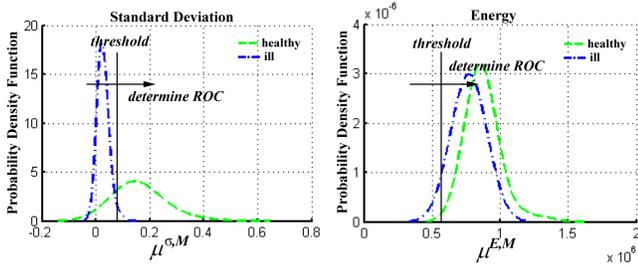


Figure 5: Probability density functions of data set features $\mu^{\sigma,M}$ and $\mu^{E,M}$ for ill and healthy persons used for determining the corresponding ROCs.

chosen so that sensitivity as well as specificity range from zero to one. The ideal ROC curve - in the sense of 100% selectivity - is given by a progression along the borders of the surrounding square which is reached for sensitivity = specificity = 1. Curves near the square's diagonal show negligible selectivity.

For comparing the classification performance of the data set features, the areas under the ROC curves (AUC) are used. An AUC of one indicates optimal classification performance whereas an AUC of one half indicates no meaningful classification. [5]

While the AUC gives information about the classification performance of each data set feature, it does not say anything about the additional information gained when several data set features are used in combination. For this purpose, the correlation coefficients between the maximum AUC data set feature and all other features are calculated. Features showing a high AUC and a low correlation increase the classification performance and can be combined into a data set feature vector that can finally be used for classification.

2.2 Estimation of Systolic & Diastolic Blood Pressure

In the following we introduce a method for automatically estimating the systolic and diastolic blood pressure from the pressure step feature σ . As shown in the results section, this feature turns out to be the best one for PAD diagnosis.

2.2.1 PSO Data Sets & Blood Pressure References

The analyzed PSOs are taken from left and right wrist measurements of 20 healthy male and female persons between the age of 20 and 60 years. This results in a total amount of $M=60$ data sets. The corresponding reference blood pressures are measured with Welly&Allyn 5200, a professional sphygmomanometer. Its measurement accuracy according to its data sheet falls below the accuracy dictated by the ANSI/AAMI standard SP10-1992 [6].

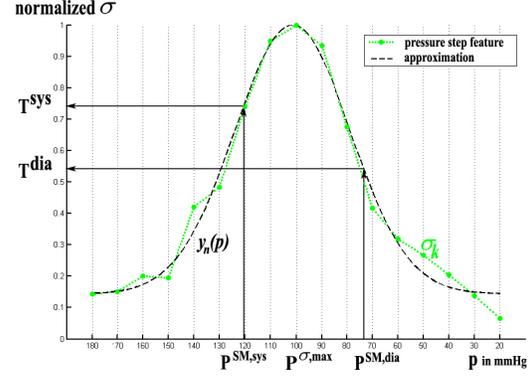


Figure 6: Normalized Gaussian like approximation $y_n(p)$ of the discrete pressure step features σ_k for one person. $y_n(p)$ determines the relationship between measured blood pressures P^{SM} and the corresponding thresholds T .

2.2.2 Feature Selection & Gaussian Approximation

The PSO measuring principle implies that oscillations are only measured for K discrete blood pressure intervals ΔP from which the pressure step feature σ is extracted. However, for accurate blood pressure estimation it is necessary to approximate the discrete feature values by a continuous curve. The Gaussian like function $y(p|P^{\sigma,max}, A, D) = A \cdot e^{-\pi A^2 (p - P^{\sigma,max})^2} + D$ is used as an analytic model that nicely describes the unimodal shape of the pressure feature σ . The parameter D represents the ordinate offset of $y(p)$ and corresponds to the minimum feature value whereas $A + D$ represents the maximum feature value. Due to the person dependent maximum values, the approximation functions need to be normalized to gain comparability between different persons, thus $y_n(p|P^{\sigma,max}, A, D) = y(p|P^{\sigma,max}, A, D) / (A + D)$. Figure 6 shows $y_n(p)$ for one person.

2.2.3 Threshold Estimation via Cross-Validation

With traditional pulse oscillation the systolic and diastolic blood pressures are deduced from the normalized oscillation hull curves at defined oscillation magnitude thresholds [7]. Transferring this principle to our approach, we need to empirically find thresholds for the Gaussian approximated and normalized pressure step feature. Evaluating the person specific normalized approximation function for the known systolic and diastolic reference blood pressures $P^{SM,sys}$ and $P^{SM,dia}$ gives the corresponding thresholds $T^{sys} = y_n(P^{SM,sys}|P^{\sigma,max}, A, D)$ and $T^{dia} = y_n(P^{SM,dia}|P^{\sigma,max}, A, D)$.

Averaging the thresholds calculated for all available reference blood pressures would lead to systolic and diastolic thresholds that are optimal for the given reference data, but would generalize poorly. To achieve a better generalization we apply 2-fold cross-validation to our data sets [5].

For this purpose, the data sets are randomly split into two parts of equal size $J = I/2$. One part is used for estimating the thresholds (training) and the other part is used for testing the estimated thresholds. The splitting is repeated $H = 5$ times. For each of the five resulting test/training groups (indexed h) the following procedure is applied:

- i. determine the systolic and diastolic thresholds $T_{h,j}^{sys}$ and $T_{h,j}^{dia}$ for all training data sets (indexed j),
- ii. average the results for the left l and right r wrist measurements to obtain the threshold candidates $T_h^{sys,l}, T_h^{dia,l}, T_h^{sys,r}$ and $T_h^{dia,r}$,
- iii. calculate the blood pressures $P_{h,j}^{sys,l}, P_{h,j}^{dia,l}, P_{h,j}^{sys,r}, P_{h,j}^{dia,r}$ using the inverse of the corresponding approximation functions,
- iv. average the left and right hand blood pressure values to obtain

| | | | | | |
|-----|------------------|-------------|----------------|----------------|-------------|
| | $\mu^{\sigma,M}$ | $\mu^{A,M}$ | $\mu^{\max,M}$ | $\mu^{\min,M}$ | $\mu^{S,M}$ |
| AUC | 0.999 | 0.998 | 0.998 | 0.992 | 0.960 |
| CC | 1.000 | 0.999 | 0.990 | -0.967 | 0.824 |
| | $\mu^{H,M}$ | $\mu^{E,M}$ | $\mu^{\mu,M}$ | $\mu^{K,M}$ | - |
| AUC | 0.897 | 0.850 | 0.530 | 0.522 | - |
| CC | 0.735 | -0.618 | 0.079 | -0.066 | - |

Table 1: AUCs for the ROC curves of all data set features $\mu^{f,M}$. Correlation coefficients (CC) between best data set feature $\mu^{\sigma,M}$ and all other data set features $\mu^{f,M}$.

the systolic blood pressures $P_{h,j}^{\text{sys}} = (P_{h,j}^{\text{sys,l}} + P_{h,j}^{\text{sys,r}})/2$ and the diastolic blood pressures $P_{h,j}^{\text{dia}} = (P_{h,j}^{\text{dia,l}} + P_{h,j}^{\text{dia,r}})/2$ for each test data set.

To figure out the thresholds $T^{\text{sys,l}}, T^{\text{dia,l}}, T^{\text{sys,r}}$ and $T^{\text{dia,r}}$ that generalize best, the blood pressures $P_{h,j}^{\text{sys}}$ and $P_{h,j}^{\text{dia}}$ of all test data sets belonging to the h -th test/training group are compared to the corresponding reference values P^{SM} . This is done by calculating the blood pressure differences $\Delta P_{h,j}^{\text{sys}} = P_{h,j}^{\text{sys}} - P_{h,j}^{\text{sys,SM}}, \Delta P_{h,j}^{\text{dia}} = P_{h,j}^{\text{dia}} - P_{h,j}^{\text{dia,SM}}$ and determining their standard deviations σ_h^{sys} and σ_h^{dia} . The thresholds for which the sum of the standard deviations is a minimum are chosen as optimal thresholds. Finally, a single systolic threshold $T^{\text{sys,opt}}$ and a single diastolic threshold $T^{\text{dia,opt}}$ is computed by averaging the optimal thresholds of the right and left hand, respectively.

2.2.4 Threshold Evaluation

In order to evaluate the general accuracy of the thresholds $T^{\text{sys,opt}}$ and $T^{\text{dia,opt}}$, they are applied to the entire data sets. As in the foregoing section, the obtained blood pressures are compared to the reference data. The arithmetic means $\bar{x}^{\text{sys}}, \bar{x}^{\text{dia}}$ (bias) and standard deviations $\sigma^{\text{sys}}, \sigma^{\text{dia}}$ of the differences are used as overall error measures.

3. RESULTS

In the following we present the results of the proposed PSO based approaches for automatic PAD diagnosis and blood pressure estimation.

3.1 Diagnosis of Peripheral Arterial Disease

Figure 7 shows the ROC curves for all analyzed data set features. $\mu^{\sigma,M}, \mu^{A,M}, \mu^{\max,M}$ and $\mu^{\min,M}$ are revealed as appropriate data set features for automatic PSO based classification of PAD positive and negative persons. They show nearly ideal ROC curve progressions that are also reflected by their ACUs, see Table 3.1.

The correlation for the best data set feature $\mu^{\sigma,M}$ to the other features is determined in order to determine whether a combination of features may improve the classification. The resulting correlation coefficients (CC) are listed in Table 3.1. The three remaining features of interest $\mu^{A,M}, \mu^{\max,M}$ and $\mu^{\min,M}$ show very high positive or negative correlations ($> |0.95|$), see Table 3.1. Because they do not provide any additional information to improve the classification result, it suffices to use the data set feature $\mu^{\sigma,M}$ for further analysis only.

The proposed algorithm is evaluated for data set features of clearly healthy and ill persons only. Nevertheless, the underlying probability density functions (see Figure 5) can be used to calculate the a posteriori probabilities for any patient to be healthy or ill, respectively, and, thus, in principle allows for the diagnosis of semi-healthy persons, too.

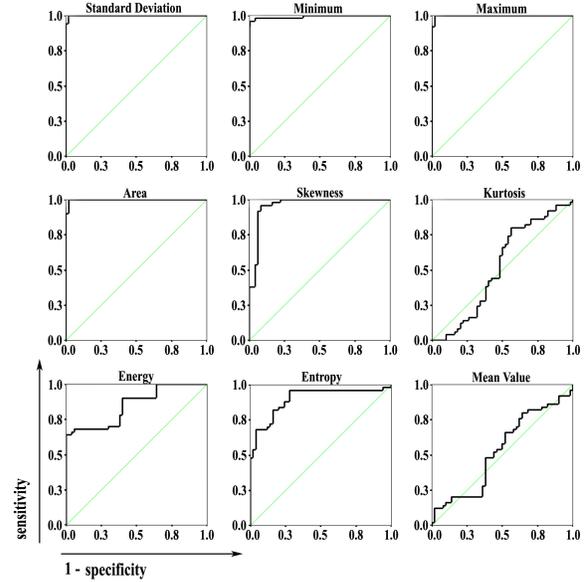


Figure 7: ROC curves of all data set features $\mu^{f,M}$. The diagonal straight line corresponds to minimum separability. ROC curves approaching the axis indicate maximum separability.

| | Left | Right |
|----------------------|--------|--------|
| $T^{\text{sys,opt}}$ | 0.7738 | 0.8026 |
| $T^{\text{dia,opt}}$ | 0.5391 | 0.5529 |

Table 2: Optimal left and right wrist thresholds for blood pressure estimation.

3.2 Estimation of Systolic & Diastolic Blood Pressure

The optimal thresholds for deducing the systolic and diastolic blood pressures of healthy persons from the approximation functions are shown in Table 3.2. As expected the difference between the estimated thresholds for the left and right wrist is negligible, which supports their averaging to obtain the final thresholds $T^{\text{sys,opt}}$ and $T^{\text{dia,opt}}$.

The requirements for blood pressure measuring accuracy given by ANSI/AAMI SP10-1992 state a systematic error \bar{x} of 5mmHg and a standard deviation σ of 8mmHg as limits for acceptance [6]. Table 3 summarizes the pressure error measures mean \bar{x} and standard deviation σ after applying the final thresholds $T^{\text{sys,opt}}$ and $T^{\text{dia,opt}}$ to all data sets and comparing the results to reference blood pressures. The measurement error of the proposed method is determined to a mean $\bar{x} < 3\text{mmHg}$ and a standard deviation $\sigma < 8\text{mmHg}$ that both fall below the limits defined in the ANSI standard [6].

| | Our method | ANSI/AAMI SP10-1992 |
|------------------------|------------|---------------------|
| \bar{x}^{sys} | 2.6900mmHg | $\leq 5\text{mmHg}$ |
| \bar{x}^{dia} | 0.0415mmHg | $\leq 5\text{mmHg}$ |
| σ^{sys} | 7.0600mmHg | $\leq 8\text{mmHg}$ |
| σ^{dia} | 6.4900mmHg | $\leq 8\text{mmHg}$ |

Table 3: Systematic errors and standard deviations when comparing blood pressure measurements using the Welly&Allyn 5200 and our method. Acceptable limits stated by ANSI/AAMI SP10-1992.

Further analysis for determining blood pressure thresholds eligible for deducing the pressures of ill persons are necessary.

4. CONCLUSION

The proposed approach for an automatic PAD diagnosis represents an interesting alternative to the currently used PAD screening tests. Due to the fact that only one pulse oscillation measurement (PSO recording) is necessary for PAD diagnosis and blood pressure estimation, this method promises to be quite fast, cheap and easy to handle. The presented results show both approaches as applicable and worth further analysis and development. We are especially interested in developing the blood pressure measurement method to be used for ill persons as well.

5. ACKNOWLEDGMENT

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